**IRISH MEDICINES BOARD ACTS 1995 AND 2006**

**MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007**

**(S.I. No.540 of 2007)**

**PPA1328/116/001**
Case No: 2064917

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

**B & S Healthcare**

**Unit 4, Bradfield Road**, **Ruislip**, **Middlesex**, **HA4 0NU**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

**Dyazide 50mg/25mg Tablets**

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **25/06/2009**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

# Part II

# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Dyazide 50mg/25mg Tablets

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50mg of Triameterene and 25mg of hydrochlorothiazide
Excipients-Contains sunset yellow (E110)
For a full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Tablet

*Product imported from the UK*:
Peach coloured, compressed, flat, circular, bevel-edged tablet with a single score line on one surface and the code 'E93' on the other.
The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

It is recommended for the treatment of mild to moderate hypertension, alone or in combination with other antihypertensive drugs. It is also recommended in the control of oedema due to cardiac failure, cirrhosis of the liver or the nephrotic syndrome. It can also be used to control the oedema associated with corticosteroid treatment, but only when the concomitant use of diuretics is considered essential.

### 4.2 Posology and method of administration

Route of administration: oral.

Adults: In hypertension
The recommended dosage is one tablet a day after the morning meal. If "Dyazide" is added to already established therapy with another antihypertensive drug, the dosage of the latter should be reduced, and later adjusted if necessary. If another antihypertensive drug is added to "Dyazide" therapy, the dosage of the latter will not normally be reduced.

Adults: In oedema
One "Dyazide" tablet a day after the morning meal.

Elderly
Dosage as for adults. "Dyazide" has been widely used and is usually well tolerated in patients over the age of 60 years. The normally occurring reduction in glomerular filtration with age should be borne in mind (see section 4.4).

### 4.3 Contraindications

Do not give "Dyazide" to patients with hyperkalaemia, progressive renal failure, increasing hepatic dysfunction. Addison's disease or known hypersensitivity to either constituent of the product.

Potassium supplements or other potassium-conversing drugs such as spironolactone or amiloride, and also ACE inhibitors, should not be given routinely with “Dyazide”. “Dyazide” should not be used during lactation or in neonates or young infants.

## 4.4 Special warnings and precautions for use

Use “Dyazide” with caution in patients with hepatic or renal insufficiency or urinary tract obstruction and in those predisposed to gout since both components can elevate uric acid levels. Thiazides can provoke hyperglycaemia and glycosuria, particularly in patients with latent diabetes, and adjustment of the dosage of hypoglycaemic agents may be necessary in diabetic patients. Dosage of concomitant cardiac glycosides may need to be adjusted.

Patients who are being treated with “Dyazide” require regular supervision with monitoring of blood and electrolyte state to avoid inadequate potassium supplementation or excessive loss of fluid. This is important in the elderly, those with renal impairment and those receiving concomitant treatment with NSAIDs (see section 4.8).

Triamterene has been found in renal stones both alone and in association with other usual calculus components. There is no evidence that stone formation is increased in patients taking triamterene-containing drugs.

These tablets contain Sunset yellow (E110), which may cause allergic reactions.

## 4.5 Interaction with other medicinal products and other forms of interaction

Thiazides reduce excretion of lithium and may thus precipitate intoxication.

In view of the potassium-retaining effect of triamterene, the concurrent use of potassium supplements, spironolactone, amiloride or Angiotensin Converting Enzyme (ACE) inhibitors should be avoided.

Concurrent use of “Dyazide” with Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) or oral hypoglycaemics may decrease their efficacy or increase their toxicity.

The concomitant administration of “Dyazide” with cardiac glycosides or hypotensive agents may necessitate adjustment of the dosage of those drugs.

## 4.6 Pregnancy and lactation

Both triamterene and thiazides have been shown to pass through the placenta in humans and also to pass into breast milk. In rare instances thrombocytopenia, pancreatitis or hypoglycaemia have been reported in new born infants of mothers treated with thiazides. The use of “Dyazide” in pregnant patients should therefore be avoided unless essential and nursing mothers should not be treated with “Dyazide”.

## 4.7 Effects on ability to drive and use machines

There are no known effects of “Dyazide” on the ability to drive and operate machinery.

## 4.8 Undesirable effects

Blood and lymphatic system: Rare cases of thrombocytopenic purpura and megaloblastic anaemia have been reported with triamterene. Rarely, blood dyscrasias including agranulocytosis, thrombocytopenia and leucopenia.

Immune system disorder: Hypersensitivity reactions, rash have been reported.
Photosensitivity can occur. Anaphylaxis is a remote possiblity. Very rare cases of SLE have been reported associated with "Dyazide".

Metabolism and nutrition disorders: Thiazide diuretics can also cause increase in plasma lipid levels.

Nervous system disorders: Dizziness, headache.

Cardiac disorder: Undesirable decrease in blood pressure (orthostatic hypotension).

Gastrointestinal disorders: Nausea, vomiting, diarrhoea, dry mouth.

Hepato-biliary disorder: Thiazides alone have caused jaundice, acute pancreatitis.
Musculoskeletal, connective tissue and bone disorder: Muscle cramps, weakness.
Renal and urinary disorder: In common with most diuretics, "Dyazide" may reduce glomerular filtration rate and cause a temporary increase in blood urea and creatinine levels: again this may also indicate excessive dosage or to be secondary to the condition under treatment.

Long-term use has confirmed that little changes have been observed infrequently, and marked fluctuations in serum potassium are uncommon.

Metabolic acidosis occasionally occurs. Electrolyte imbalance may also indicate excessive dosage or to be secondary to the condition under treatment.

Renal failure, reversible on stopping treatment has been reported very rarely and has been due to acute interstitial nephritis or an interaction between triamterene and some NSAISs.

## 4.9 Overdose

Symptoms of electrolyte imbalance, hypertension, gastrointestinal disturbance and muscular weakness may occur. Treatment consists of the induction of vomiting and/or gastric lavage, correction of fluid depletion and electrolyte imbalance, and symptomatic and supportive therapy. If hypertension persists after adequate fluid replacement, dopamine may be used and expert advice sought. Cardiac rhythm should be monitored and appropriate measure to be taken to correct hyperkalaemia as necessary. Renal dialysis may be some benefit in cases of severe overdosage.

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

“Dyazide” contains triamterene and hydrochlorothiazide. Triamterene is a potassium conversing diuretic thought to act by directly inhibiting the exchange of sodium for potassium and hydrogen in the distal renal tubule.
Hydrochlorothiazide is a thiazide diuretic which reduces the reabsorption of electrolytes from the renal tubules, thereby increasing the excretion of sodium and chloride ions, and consequently of water. Potassium ions are excreted to a lesser extent.

## 5.2 Pharmacokinetic properties

Onset of diuresis takes place within one hour, peak hours at two to three hours and tapers off during the subsequent seven to nine hours.

Triamterene is incompletely but fair rapidly absorbed from the gastrointestinal tract. It has been estimated to have plasma half-life of about two hours. It is extensively metabolised and is mainly excreted in the form of metabolites with some unchanged triamterene; variable amounts are also excreted in the bile. Hydrochlorothiazide is incompletely but fairly rapidly absorbed from the gastro-intestinal tract. It is excreted in the urine.

## 5.3 Preclinical safety data

Recent review of pre-clinical animal studies has suggested that triamterene is carcinogenic in both sexes of mice and in male rats. Such effects have not been reported in human clinical use.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Maize starch
Povidone 30
Sodium lauryl Sulphate
Sunset Yellow (E110)
Sodium Starch Glycollate Type A
Magnesium Stearate
Purified Water

## 6.2 Incompatibilities

Not applicable

## 6.3 Shelf Life

The shelf-life expiry date of this product is the date shown on the container and outer package of the product on the market in the country of origin.

## 6.4 Special precautions for storage

Do not store above 25°C
Store in the original package in order to protect from light

## 6.5 Nature and contents of container

Opaque PVC/PVdC/Aluminium foil blister pack in an overlabelled outer container containing 30 tablets

## 6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements

# 7 Parallel Product Authorisation Holder

B & S Healthcare
Unit 4, Bradfield Road
Ruislip,
Middlesex
TW3 3JA
United Kingdom

# 8 Parallel Product Authorisation Number

PPA 1328/116/1

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 25th June 2009

## 10 DATE OF REVISION OF THE TEXT